Clinical Policy: Deferiprone (Ferriprox)

Reference Number: ERX.SPA.92
Effective Date: 10.01.16
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Deferiprone (Ferriprox®) is an iron chelator.

FDA Approved Indication(s)
Ferriprox is indicated for the treatment of transfusional iron overload in adult and pediatric patients (tablets: 8 years of age and older; oral solution: 3 years of age and older) with thalassemia syndromes, sickle cell disease, or other anemias.

Limitation(s) of use: Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with myelodysplastic syndrome or in patients with Diamond Blackfan anemia.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Ferriprox is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Transfusional Iron Overload (must meet all)**:**

1. Diagnosis of transfusional iron overload due to one of the following (a, b, or c):
   a. Thalassemia syndromes;
   b. Sickle cell disease;
   c. Other anemia;
2. Member meets one of the following (a or b):
   a. For Ferriprox tablets: Age ≥ 8 years;
   b. For Ferriprox oral solution: Age ≥ 3 years
3. Transfusion history of ≥ 100 mL/kg of packed red blood cells (e.g., ≥ 20 units of packed red blood cells for a 40 kg person) and a serum ferritin level > 1,000 mcg/L;
4. Failure of deferoxamine (Desferal®) and deferasirox (Exjade®, Jadenu®), unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for deferoxamine and deferasirox*
5. Dose does not exceed 99 mg/kg per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Transfusional Iron Overload (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;

2. Current documentation (within the past 30 days) shows serum ferritin level ≥ 500 mcg/L;
3. If request is for a dose increase, new dose does not exceed 99 mg/kg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
ANC: absolute neutrophil count
DFO-DFP: deferiprone-deferoxamine
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
deferoxamine (Desferal®)	1000 mg x 1 dose, then 500 mg Q4 hr x 2 doses PRN, then 500 mg Q4-12 hr PRN.* **IM route if patient not in shock; IV infusion limited to patients in cardiovascular collapse.*	6000 mg/24 hr
	1000-2000 mg SC QD (20-40 mg/kg/day) over 8-24 hours.	See dosing regimen
	20-40 mg/kg IV daily (children*) and 40-50 mg/kg IV daily (adults) for 5-7 days per week. **Average dose should not exceed 40 mg/kg/day until growth has ceased.*	40 mg/kg/day (children) 60 mg/kg/day (adults)
	500-1000 mg IM/day.	1000 mg/day
deferasirox (Exjade®)	20 to 40 mg/kg (calculated to the nearest whole tablet) PO QD	40 mg/kg/day
deferasirox (Jadenu®)	14 mg/kg (calculated to the nearest whole tablet) PO QD	28 mg/kg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Box Warnings;

- Contraindication(s): hypersensitivity to deferiprone or to any of the excipients in the formulation
- Boxed warning(s): agranulocytosis/neutropenia

Appendix D: Combination Therapy
A multicentre randomized open-label trial was designed to assess the effectiveness of long-term sequential deferiprone-deferoxamine (DFO-DFP) versus DFP alone to treat thalassaemia major. The decrease of serum ferritin levels during the treatment period was statistically significantly higher in sequential DFP-DFO patients compared with DFP-alone patients (P = 0.005). Kaplan-Meier survival analysis for the two chelation treatments did not show any statistically significant differences (long-rank test, P = 0.3145). Evidence exists to support the use of combination therapy with Ferriprox (deferiprone) and Desferal (deferoxamine) in patients with severe iron overload or overt iron-related morbidity.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Transfusional iron overload	75 mg/kg PO in 2 or 3 divided doses for a total daily dose of 75 to 99 mg/kg/day in 2 or 3 divided doses	99 mg/kg/day

VI. Product Availability

- Oral solution: 100 mg/mL
- Tablets: 500 mg with functional scoring, 1,000 mg (three times a day) with functional scoring, 1,000 mg (twice a day) with functional scoring

VII. References

1. Ferriprox Tablets Prescribing Information. Rockville, MD: ApoPharma USA, Inc.; April 2021. Available at www.ferriprox.com. Accessed May 13, 2021.
2. Ferriprox Oral Solution Prescribing Information. Rockville, MD: ApoPharma USA, Inc.; April 2021. Available at http://www.ferriprox.com/us/pdf/ferriprox_full_pi.pdf. Accessed May 13, 2021.
3. Desferal Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2020. Available at https://dailymed.nlm.nih.gov/dailymed/. Accessed May 13, 2021.
4. Exjade Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020. Available at http://www.us.exjade.com/. Accessed May 13, 2021.
5. Jadenu Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020. Available at https://www.jadenu.com/. Accessed May 13, 2021.
6. Musallam KM, Angastiniotis M, Eleftheriou A, Porter JB. Cross-talk between available guidelines for the management of patients with beta-thalassemia major. Acta Haematol. 2013; 130: 64-73. DOI: 10.1159/000345734.
7. Hoffbrand AV, Taher A, Cappellini MD. How I treat tranfusional iron overload. Blood. November 1, 2012; 120(18): 3657-3669.
8. Maggio A, Vitrano A, Capra M, et al. Long-term sequential deferiprone-deferoxamine versus deferiprone alone for thalassaemia major patients: a randomized clinical trial. Br J Haematol. 2009;145:245-54.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Added max dose. Removed preferencing for Exjade, Jadenu, or Desferal as these agents are not on the formulary. Added "current documentation" defined as "within the last 30 days" for follow-up serum ferritin levels.	07.17	08.17
3Q 2018 annual review: no significant changes; approval periods changed from 3/6 months to 6/12 months; references reviewed and updated.	04.27.18	08.18
3Q 2019 annual review: no significant changes; references reviewed and updated.	05.14.19	08.19
RT4: added new 1,000 mg tablet to Section VI.	08.07.19	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2020 annual review: added redirection to both deferoxamine and deferasirox per clinical guidance; added new tri-scored 1,000 mg tab formulation; references reviewed and updated.	06.04.20	08.20
3Q 2021 annual review: RT4: added new indication for sickle cell and other anemias transfusional iron overload with pediatric expansions; references reviewed and updated.	05.13.21	08.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.